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ORIGINAL RESEARCH

A Cohort Study on Systemic Immune-Inflammation Index and Its Longitudinal Change in Relation to Colorectal Adenoma Recurrence

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Objective: This study aimed to investigate the associations of both baseline systemic immune-inflammation index (SII) and, more importantly, its longitudinal change (ΔSII) during follow-up with the risk of advanced colorectal neoplasia (ACRN) recurrence after endoscopic resection of colorectal adenomas.

Methods: Clinical data from 1855 patients diagnosed with colorectal adenomas and undergoing resection at Hospital between January 2017 and August 2023 were analyzed. Patients were classified into Q1–Q4 groups based on baseline SII quartiles and into three groups according to ΔSII. Cox proportional hazards regression models, restricted cubic spline (RCS) analysis, Kaplan-Meier curves, receiver operating characteristic (ROC) curve, subgroup analysis, sensitivity analyses were used to evaluate associations.

Results: After an average follow-up of 3.4 years, 166 patients (8.95%) experienced ACRN recurrence. After fully adjusting for variables, Cox proportional hazards regression analysis revealed that the group with the highest baseline SII (Q4) had a 1.75-fold increased risk of ACRN recurrence compared to Q1 (HR, 1.75; 95% *CI*, 1.12–2.75). Patients with a significant SII increase (ΔSII > 0.15) had a 1.88-fold higher recurrence risk than those with a stable SII (−0.15 ≤ ΔSII ≤0.15) (HR, 1.88; 95% *CI*, 1.24–2.86). Dose-response curves indicated a rising ACRN recurrence risk when ΔSII ranged from 0.008 to 1.103, followed by a declining trend for ΔSII ≥ 1.103 (*P*-overall=0.003, *P*-nonlinear=0.005). ROC analysis showed that incorporating either SII levels or ΔSII grouping improved the predictive ability (AUC) for postoperative recurrence. Subgroup analyses confirmed that both a high baseline SII (Q4) and a significant SII increase (ΔSII > 0.15) were associated with elevated recurrence risk, particularly among males and older adults.

Conclusion: Not only baseline SII but also ΔSII during follow-up serves as a significant and independent predictor for ACRN recurrence. Monitoring the longitudinal change of SII may provide incremental clinical value for optimizing personalized surveillance strategies after endoscopic resection.

Keywords: systemic immune-inflammation index, colorectal cancer, advanced colorectal neoplasia, recurrence, cohort study

Introduction

Colorectal Cancer (CRC) is a highly heterogeneous primary epithelial malignancy with diverse risk factors, posing a significant threat to human health. According to the Global Cancer Statistics 2022 (GLOBOCAN 2022), CRC ranks as the third most common cancer globally in terms of incidence and the second leading cause of cancer-related mortality, surpassed only by lung cancer. Without effective interventions, the incidence and mortality rates of CRC are expected to rise persistently, with new cases and deaths expected to reach 3.2 million and 1.6 million, respectively, by 2040.[1,2] CRC predominantly arises from the progression of colorectal adenomas, which are recognized as the primary precancerous

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lesions.[3] Currently, the risk of metachronous advanced colorectal neoplasia (ACRN) has been established as a surrogate marker for CRC risk.[4] Studies have confirmed that early detection and endoscopic resection of colorectal adenomas significantly reduce CRC incidence, making this approach a cornerstone for CRC prevention.[5] However, there is a certain risk of recurrence following endoscopic resection of colorectal adenomas, with reported recurrence rates of ACRN ranging from 5.6% to 37.4% within 3–5 years after polypectomy,[6,7] underscoring the need for vigilant long-term surveillance.

The Systemic Immune-Inflammation Index (SII), calculated as (platelets × neutrophils / lymphocytes), is a composite inflammatory biomarker that integrates three independent hematologic parameters: lymphocytes, neutrophils, and platelet count. This index reflects the balance between pro-tumor inflammatory cells and anti-tumor immune cells. Elevated SII values indicate a heightened systemic inflammatory state and are often associated with poor prognosis in cancer patients.[8] In recent years, SII has gained significant attention for its prognostic utility in various malignancies, including gastric, lung, and esophageal cancers.[9–11] Emerging evidence highlights a correlation between elevated SII levels and adverse survival outcomes across multiple cancers.[12–15] Specifically, in colorectal cancer (CRC), numerous studies have confirmed that higher SII is significantly linked to worse overall survival (OS), disease-free survival (DFS), progression-free survival (PFS), and recurrence-free survival (RFS).[16,17] Furthermore, growing research extends the relevance of inflammatory indices to recurrence risk in the broader spectrum of colorectal neoplasia. For instance, a recent study has also delved into the prognostic significance of specific cellular components within the local tumor immune microenvironment.[18] This suggests that both the systemic inflammatory status and the specific local immune landscape of the tumor play crucial roles in the progression and recurrence of colorectal neoplasia. However, the specific role of SII levels and their longitudinal changes in predicting the recurrence of ACRN after colorectal adenoma resection remains unclear. Limited evidence exists regarding the association between SII changes and ACRN recurrence post-resection, highlighting a critical research gap. This cohort study aims to address this gap by investigating the relationship between baseline SII levels, longitudinal SII change, and ACRN recurrence after adenoma resection. Our findings may provide novel insights into risk stratification and surveillance strategies, ultimately improving the prediction and prevention of ACRN recurrence in clinical practice.

Materials and Methods

Study Population

This study selected 15259 patients who underwent ≥3 complete colonoscopies at the First Affiliated Hospital of Zhengzhou University between January 2016 and August 2023. The exclusion criteria were as follows: (1) Age <18 years or missing age data at baseline (n=132); (2) History of colorectal cancer, adenomas, colectomy, or baseline colorectal cancer diagnosis (n=3050); (3) Comorbid inflammatory bowel disease, familial adenomatous polyposis, hamartomatous polyposis, or other colorectal disorders (n=1164); (4) Missing baseline pathological reports or epidemiological data (n=561); (5) Absence of critical laboratory data during baseline or follow-up (n=2939); (6) Follow-up after resection of colorectal adenoma without pathological report or follow-up <6 months (n=5558).

Colonoscopy was performed by trained and experienced endoscopists, with successful intubation to the cecum and a withdrawal time ≥6 minutes. All detectable lesions were resected and sent to the pathology department. Histological diagnosis of adenomas was independently reviewed by two specialized pathologists. Discordant cases were adjudicated by a senior pathologist to determine the final diagnosis. Ultimately, 1855 patients were included in the cohort study. The study was approved by the Ethics Review Committee of the First Affiliated Hospital of Zhengzhou University (2022-KY-0018-002), and all participants signed informed consent forms.

Information Gathering

This study extracted baseline information, including the exposure variable (SII), outcome variable (ACRN recurrence), and covariates such as: Demographics: age (young: 18–44 years; middle-aged: 45–59 years; elderly: ≥60 years), sex (male/female). Lifestyle factors: smoking history (yes/no), alcohol consumption history(yes/no). Adenoma characteristics: number (1/2/≥3), size (1–5/6–9/≥10mm), histology (tubular adenoma / tubulovillous or villous adenoma), location

(distal colon or rectum/proximal colon/both), grade of adenoma dysplasia (low-grade/high-grade dysplasia). Symptoms: abdominal pain (yes/no), abdominal distension (yes/no), changes in bowel habits(yes/no), change in stool consistency (yes/no), and clinical symptoms (0/1/≥2). Comorbidities: diabetes (yes/no), hypertension (yes/no), hyperlipidemia (yes/no), cancer history(yes/no), and family history(yes/no).

Body mass index (BMI): underweight: <18.5 kg/m^2; normal: 18.5–23.9 kg/m^2; overweight: ≥24.0 kg/m^2), measured by clinicians using standardized protocols (barefoot, light clothing). Blood pressure was measured using an Omron sphygmomanometer. Participants abstained from alcohol, caffeine, and exercise for 30 minutes prior to measurement. Seated SBP and DBP were recorded three times at 2-minute intervals, with the average value used for analysis. Fasting venous blood samples were collected and analyzed using a Roche automated biochemical analyzer for glucose, lipid profiles, and complete blood counts (2016–2023 data). Neutrophil, lymphocyte, and platelet counts were utilized to calculate SII.

SII grouping: Quartile-based categorization: Q1 group: SII <275.60×10^9/L, Q2 group: 275.60–368.07×10^9/L, Q3 group: 368.07–513.62×10^9/L, Q4 group: ≥513.62×10^9/L.

ΔSII: Defined as (final SII−baseline SII) / baseline SII (negative values indicate SII reduction). Patients were stratified into: ΔSII <-0.15 group, $-0.15 \leq \Delta SII \leq 0.15$ group, and ΔSII >0.15 group. The ΔSII was calculated using measurements from baseline and the final follow-up, providing a practical measure of the inflammatory trend over time.This two-point method balances the need for longitudinal data with the practical realities of clinical practice.

Cancer history: Participants were categorized based on their self-reported history of any malignancy.

Hypertension: SBP ≥140 mmHg and/or DBP ≥90 mmHg on three non-consecutive measurements, antihypertensive medication use, or prior diagnosis.

Diabetes: Fasting glucose ≥7.0 mmol/L, random glucose ≥11.1 mmol/L, HbA1c ≥6.5%, or antidiabetic treatment.

Hyperlipidemia: TC ≥6.2 mmol/L, TG ≥2.3 mmol/L, HDL-C <1.0 mmol/L, or lipid-lowering therapy.

Follow-Up and Outcome Definitions

Patients initially diagnosed with colorectal adenomas via colonoscopy and undergoing resection were re-examined within 1 year to identify potential missed lesions. Subsequent surveillance was conducted for up to 77.5 months, with ACRN recurrence occurring ≥6 months post-resection defined as the endpoint. During the follow-up period, 166 cases of ACRN recurrence were documented.

ACRN was defined as advanced adenomas (meeting ≥1 of the following criteria: diameter >10mm, presence of villous components, or high-grade intraepithelial neoplasia)[19] or CRC.

Statistical Analysis

Data analysis was performed using R 4.3.3 and SPSS 27.0 software. In this study, continuous variables that followed a normal distribution are presented as mean ± standard deviation (SD), continuous variables with a skewed distribution are summarized as the median (Q1, Q3), and categorical data were expressed as n (%). Differences in categorical variables between groups were assessed using the Chi-square (χ^2) test.

SII levels and their categorized groupings were treated as independent variables, with the occurrence of ACRN was the dependent variable.The association of SII levels and their changes with ACRN recurrence after adenoma resection was first visualized using Kaplan-Meier curves, with differences examined by the Log rank test. Subsequently, Cox proportional hazards regression models were employed to quantify these relationships.Three models were progressively developed: Model 1 (unadjusted) estimated the initial association; Model 2 was adjusted for age, a well-established risk factor in colorectal tumorigenesis; Model 3 was further adjusted for key clinicopathological characteristics, including adenoma number, size, histology, location, dysplasia grade, and family history, to evaluate the independent predictive value of SII after accounting for these confounders. Additionally, the ΔSII grouping was used as the independent variable, and four models were progressively constructed: Similarly, Model 1 was unadjusted, Model 2 was adjusted for age, and Model 3 was adjusted for the same clinicopathological features listed above. Model 4 was then constructed by additionally adjusting for baseline SII grouping on the basis of Model 3, in order to determine whether the longitudinal change in SII provided independent predictive information beyond the baseline level alone. Results are expressed as

hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). The dose-response relationships of continuous baseline SII and ΔSII with ACRN risk were flexibly modeled using restricted cubic splines (RCS). Independent risk factors were identified through multivariate analysis in the Cox proportional hazards regression model, followed by stepwise regression and the construction of a nomogram.

The predictive performance of the nomogram was evaluated by plotting receiver operating characteristic (ROC) curves and calculating the area under the curve (AUC). Subgroup analyses were conducted by gender and age to assess the consistency of the main findings. Finally, a sensitivity analysis was performed by excluding individuals diagnosed with ACRN recurrence within 6 months of baseline to ensure the robustness of the results. All statistical tests were two-sided (α=0.05), and *P-value* <0.05 was considered statistically significant.

Results

Demographics and Characteristics of the Participants

This study enrolled a total of 1855 participants. After a mean follow-up period of 3.4 years, 166 patients developed ACRN, yielding an incidence rate of 8.95%. The SII values ranged from 43.8 to 1978.95×10^9/L, while ΔSII varied between −0.01 and 2.9 (Figure S1). Baseline characteristics of participants stratified by SII quartiles revealed that the Q4 group (highest quartile) exhibited significantly higher proportions of males (1299, 66.3%), individuals aged ≥60 years, those with high-grade epithelial neoplasia, altered bowel habits, ≥1 clinical symptom, hypertension, hyperlipidemia, and cancer history compared to Q1-Q3 groups (all P <0.05). Statistically significant differences were observed across Q1-Q4 in adenoma dysplasia grade, abdominal pain, bowel habit changes, number of clinical symptoms, hypertension, hyperlipidemia, cancer history, and BMI (all P <0.05, Table 1). Furthermore, patients were categorized into recurrence and non-recurrence groups based on postoperative ACRN development. Significant intergroup differences emerged in baseline characteristics including age, adenoma number, adenoma size, adenoma histology, adenoma location, adenoma dysplasia grade, family history, ΔSII, and ΔSII grouping (all P <0.05, Table S1).

Table 1 Baseline Characteristics of the Study Participants

Variables	Overall (n=1855)	SII Grouping				χ^2	*P* value
		Q1 (n=464)	Q2 (n=463)	Q3 (n=464)	Q4 (n=464)		
Sex, No. (%)						0.95	0.813
Female	626	158(34.1)	153(33.0)	151(32.5)	164(35.3)		
Male	1229	306(65.9)	310(67.0)	313(67.5)	300(64.7)		
Age, No. (%)						6.63	0.357
18-44	294	67(14.4)	66(14.3)	80(17.2)	81(17.5)		
45-60	940	251(54.1)	236(51.0)	235(50.6)	218(47.0)		
≥60	621	146(31.5)	161(34.8)	149(32.1)	165(35.6)		
Smoking history, No. (%)						2.35	0.503
No	1519	390(84.1)	380(82.1)	374(80.6)	375(80.8)		
Yes	336	74(15.9)	83(17.9)	90(19.4)	89(19.2)		
Alcohol consumption history, No. (%)						1.20	0.754
No	1394	356(76.7)	346(74.7)	342(73.7)	350(75.4)		
Yes	461	108(23.3)	117(25.3)	122(26.3)	114(24.6)		
BMI, No. (%)						25.71	<0.001
<18.5kg/m^2	46	19(4.1)	5(1.1)	10(2.2)	12(2.6)		
18.5–23.9kg/m^2	718	198(42.7)	181(39.1)	146(31.5)	193(41.6)		
>23.9kg/m^2	1091	247(53.2)	277(59.8)	308(66.4)	259(55.8)		
Adenoma number, No. (%)						2.15	0.906
1	1437	361(77.8)	362(78.2)	364(78.4)	350(75.4)		
2	320	77(16.6)	79(77.8)	75(16.2)	89(19.2)		
≥3	98	26(5.6)	22(77.8)	25(5.4)	25(5.4)		

(*Continued*)

Table 1 (Continued).

Variables	Overall (n=1855)	SII Grouping				χ^2	*P* value
		Q1 (n=464)	Q2 (n=463)	Q3 (n=464)	Q4 (n=464)		
Adenoma size, No. (%)						6.64	0.356
1-5mm	929	247(53.2)	233(50.3)	225(48.5)	224(48.3)		
6-10mm	465	108(23.3)	123(26.6)	125(26.9)	109(23.5)		
>10mm	461	109(23.5)	107(23.1)	114(24.6)	131(28.2)		
Adenoma histology, No. (%)						2.57	0.464
Tubular adenoma	1294	321(69.2)	316(68.3)	324(69.8)	303(65.3)		
Tubulovillous adenoma or villous adenoma	591	143(30.8)	147(31.7)	140(30.2)	161(34.7)		
Adenoma location, No. (%)						1.43	0.964
Distal colon or rectum	860	218(47.0)	212(45.8)	221(47.6)	209(45.0)		
Proximal colon	741	180(38.8)	191(41.3)	182(39.2)	188(40.5)		
Both	254	66(14.2)	60(13.0)	61(13.1)	67(14.4)		
Adenoma dysplasia grade, No. (%)						16.81	<0.001
Low-grade dysplasia	1712	430(92.7)	442(95.5)	430(92.7)	410(88.4)		
High-grade dysplasia	143	34(7.3)	21(4.5)	34(7.3)	54(11.6)		
Abdominal pain, No. (%)						14.49	0.002
No	1379	352(75.9)	370(79.9)	325(70.0)	332(71.6)		
Yes	476	112(24.1)	93(20.1)	139(30.0)	132(28.4)		
Abdominal distension, No. (%)						0.49	0.922
No	1670	415(89.4)	419(90.5)	416(89.7)	420(90.5)		
Yes	185	49(10.6)	44(9.5)	48(10.3)	44(9.5)		
Change in bowel habits, No. (%)						28.37	<0.001
No	1699	437(94.2)	438(94.6)	425(91.6)	399(86.0)		
Yes	156	27(5.8)	25(5.4)	39(8.4)	65(14.0)		
Change in stool consistency, No. (%)						0.18	0.980
No	1698	424(91.4)	425(91.8)	423(91.2)	426(91.8)		
Yes	157	40(8.6)	38(8.2)	41(8.8)	38(8.2)		
Clinical symptoms, No. (%)						18.92	0.004
0	1121	295(63.6)	309(66.7)	261(56.3)	256(55.2)		
1	526	118(25.4)	113(24.4)	147(31.7)	148(31.9)		
≥2	208	51(11.0)	41(8.9)	56(12.1)	60(12.9)		
Diabetes, No. (%)						5.01	0.171
No	1512	388(83.6)	373(80.6)	386(83.2)	365(78.7)		
Yes	343	76(16.4)	90(19.4)	78(16.8)	99(21.3)		
Hypertension, No. (%)						17.98	<0.001
No	1366	362(78.0)	359(77.5)	331(71.3)	314(67.7)		
Yes	489	102(22.0)	104(22.5)	133(28.7)	150(32.3)		
Hyperlipemia, No. (%)						16.06	0.001
No	1510	405(87.3)	364(78.6)	378(81.5)	363(78.2)		
Yes	345	59(12.7)	99(21.4)	86(18.5)	101(21.8)		
Cancer history, No. (%)						8.11	0.044
No	1723	429(92.5)	441(95.2)	433(93.3)	420(90.5)		
Yes	132	35(7.5)	22(4.8)	31(6.7)	44(9.5)		
Family history, No. (%)						2.98	0.394
No	1776	438(94.4)	447(96.5)	446(96.1)	445(95.9)		
Yes	79	26(5.6)	16(3.5)	18(3.9)	19(4.1)		

Abbreviations: BMI, body mass index; Q1, Q1 group (SII <275.60×10^9/L); Q2, Q2 group (275.60≤ SII<368.07×10^9/L); Q3, Q3 group (368.07≤ SII <513.62×10^9/L); Q4, Q4 group (SII ≥513.62×10^9/L).

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ACRN Recurrence Rates Stratified by SII Levels and Changes

The recurrence densities of colorectal adenoma after resection in SII grouping were 1.73, 2.16, 2.37, and 2.70 per 100 person-years (PYs), respectively, with a significant ascending trend in incidence across Q1-Q4 ($P_{for\ trend}$ = 0.035). For ΔSII grouping recurrence densities were 2.75, 1.73, and 4.47/100 PYs, respectively, showing statistically significant intergroup differences (P<0.001). The ΔSII >0.15 group exhibited significantly higher recurrence rates compared to the ΔSII <-0.15 and −0.15 ≤ ΔSII ≤0.15 groups, with the lowest incidence observed in the −0.15 ≤ ΔSII ≤ 0.15 group ($P_{for\ trend}$ <0.001; Table S2).

To further evaluate the association between SII levels, their longitudinal changes, and postoperative ACRN recurrence, Kaplan-Meier curves with Log rank tests were performed, as shown in Figure 1. The analysis revealed statistically significant differences in cumulative ACRN incidence across SII grouping (P=0.014), with the Q4 group demonstrating higher recurrence rates compared to Q1-Q3 (Figure 1A). In contrast, no significant differences were observed among ΔSII grouping (P=0.086; Figure 1B). The residual diagram of ΔSII grouping is shown in Figure S2.

The Risk of ACRN Recurrence After Colorectal Adenoma Resection with SII Levels and Changes

Univariable Cox proportional hazards regression analysis identified variables significantly associated with ACRN recurrence (P<0.05; Table S3). Subsequent analyses were conducted using postoperative ACRN recurrence as the dependent variable and SII grouping (with Q1 as the reference) as the independent variable. In both unadjusted and adjusted models (controlling for age, adenoma number, adenoma size, adenoma histology, adenoma location, adenoma dysplasia grade, and family history), elevated baseline SII were consistently associated with increased ACRN recurrence risk (P <0.05; Table 2). Specifically, the Q4 group exhibited a 1.90-fold higher risk compared to Q1 in the unadjusted model (HR, 1.90; 95% *CI*, 1.22–2.97; P=0.005). After adjustment, the risk remained significantly elevated (adjusted HR, 1.75; 95% *CI*, 1.12–2.75; P=0.014).

When analyzing ΔSII grouping (with −0.15 ≤ ΔSII ≤ 0.15 as the reference), both unadjusted and adjusted models (adjusted for age, adenoma number, adenoma size, adenoma histology, adenoma location, adenoma dysplasia grade, family history, and SII grouping), the ΔSII>0.15 group demonstrated progressively higher recurrence risks across sequential adjustment models. In the fully adjusted model, ΔSII >0.15 group had a 1.88-fold increased risk (HR, 1.88;

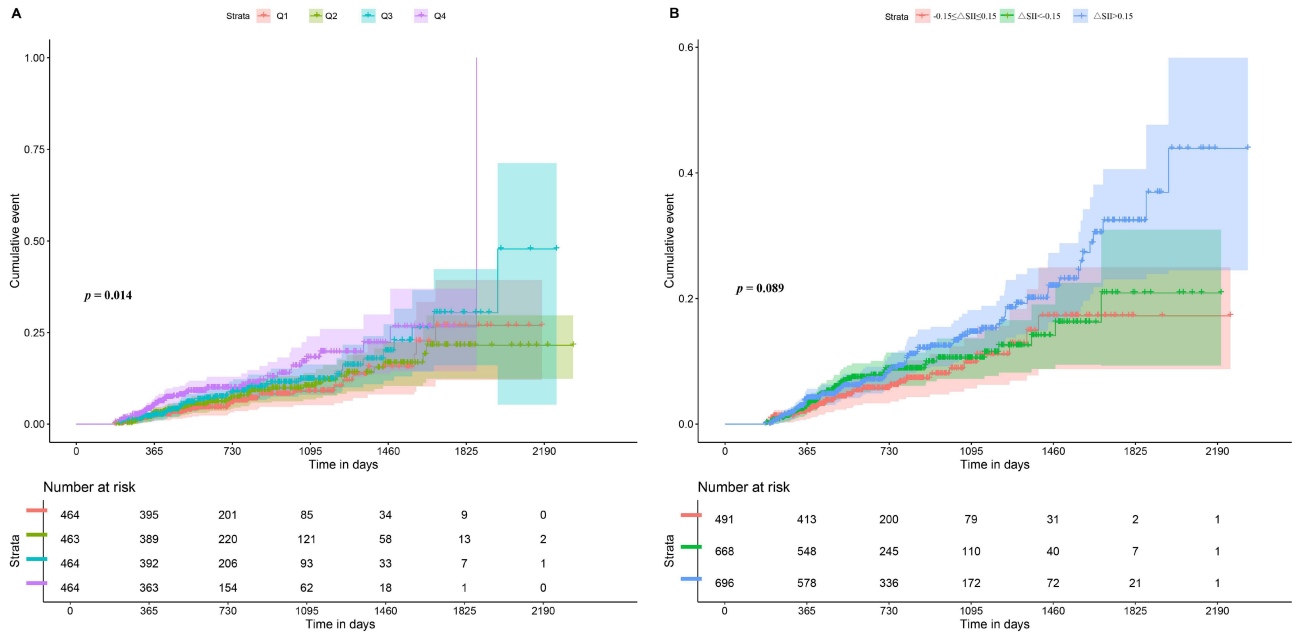

Figure 1 Kaplan-Meier curves for postoperative ACRN recurrence stratified by SII and ΔSII. (**A**) Cumulative ACRN incidence across SII grouping (Q1-Q4). (**B**) Cumulative ACRN incidence by ΔSII grouping.

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Table 2 ACRN Recurrence After Colorectal Adenoma Resection by SII Levels and Changes

Variables	Model 1		Model 2		Model 3		Model 4	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Baseline SII	1.00 (1.00–1.00)	<0.001	1.00 (1.00–1.00)	<0.001	1.00 (1.00–1.00)	0.008		
SII grouping								
Q1 group	Ref		Ref		Ref			
Q2 group	1.10 (0.69–1.75)	0.691	1.09 (0.68–1.73)	0.729	1.14 (0.72–1.82)	0.578		
Q3 group	1.38 (0.87–2.17)	0.169	1.37 (0.87–2.16)	0.179	1.37 (0.87–2.17)	0.178		
Q4 group	1.90 (1.22–2.97)	0.005	1.90 (1.21–2.96)	0.005	1.75 (1.12–2.75)	0.014		
$P_{for\ trend}$		0.002		0.002		0.009		
ΔSII grouping								
ΔSII<-0.15 group	1.21 (0.77–1.88)	0.421	1.20 (0.77–1.87)	0.417	1.17 (0.75–1.82)	0.514	0.94 (0.59–1.49)	0.783
−0.15≤ΔSII≤0.15 group	Ref		Ref		Ref		Ref	
ΔSII>0.15 group	1.54 (1.02–2.32)	0.039	1.54 (1.02–2.31)	0.040	1.69 (1.12–2.56)	0.013	1.88 (1.24–2.85)	0.003
$P_{for\ trend}$		0.030		0.030		0.007		0.001

Notes: Model 1: Unadjusted; Model 2: Adjusted for age; Model 3: Adjusted for age, adenoma number, adenoma size, adenoma histology, adenoma location, adenoma dysplasia grade, and family history; Model 4: Further adjusted for SII grouping in addition to all covariates in Model 3.
Abbreviations: HR, hazard ratio; CI, confidence interval; Q1 group, SII <275.60×10^9/L; Q2 group, 275.60≤ SII <368.07×10^9/L; Q3 group, 368.07≤ SII <513.62×10^9/L; Q4 group, SII ≥513.62×10^9/L.

95% *CI*, 1.24–2.85; *P*=0.003) compared to the reference group (Table 2). Notably, when both SII grouping and ΔSII grouping were included in a combined multivariable model, both variables independently predicted ACRN recurrence (*P*<0.05; Figure S3).

Dose-Response Relationship Between Baseline SII and ΔSII and ACRN Recurrence After Colorectal Adenoma Resection

Figure 2 shows the RCS curves between baseline SII and ΔSII and ACRN recurrence after colorectal adenoma resection. Using baseline SII as a continuous variable and adjusting for age, adenoma number, adenoma size, adenoma histology, adenoma location, adenoma dysplasia grade, and family history, the analysis revealed no statistically significant overall association between baseline SII and ACRN recurrence (*P*-overall=0.078), as shown in Figure 2A. Further adjusted for age, adenoma number, adenoma size, adenoma histology, adenoma location, adenoma dysplasia grade, family history, and SII grouping, there was a significant statistical significance between the ΔSII and the recurrence of ACRN after surgery (*P*-overall=0.003), and an inverted U-shaped trend between the rate of ΔSII and the recurrence of ACRN after surgery (*P*-nonlinear=0.005). When the ΔSII is between −0.558 and 0.0008, it acts as a protective factor for ACRN recurrence after surgery. As the ΔSII increases from 0.0008, the risk of ACRN recurrence after colorectal adenoma resection shows an increasing trend, with the ΔSII becoming a risk factor for ACRN recurrence. However, when the ΔSII reaches 1.103, the relationship between the ΔSII and the risk of ACRN recurrence after surgery begins to show a decreasing trend. This may be because, when the ΔSII is ≥1.103, there are only 138 patients, accounting for just 7.40% of the total population, as shown in Figure 2B.

Predictive Value of SII Levels and Changes for Postoperative ACRN Recurrence

Variables identified as significant in univariable Cox proportional hazards regression analyses were incorporated into multivariable models using a stepwise regression approach. Significant predictors from the final multivariable Cox model were used to construct a prognostic nomogram (Figure S4). Figure 3 showed the ROC curves based on the nomogram to assess the predictive value of SII levels and changes. Specifically, the area under the curve (AUC) values with adenoma number, adenoma size, and adenoma dysplasia grade were 0.765, 0.694, and 0.693 for predicting 1, 2, and 3-year postoperative ACRN recurrence, respectively (Figure 3A). Inclusion of SII grouping improved predictive accuracy, increasing AUC values to 0.781 and 0.695 for 1- and 3-year recurrence (Figure 3 (A1, A3)), while the AUC for 2-year recurrence remained essentially unchanged (Figure 3 (A2)). When adjusted for age, adenoma characteristics (number,

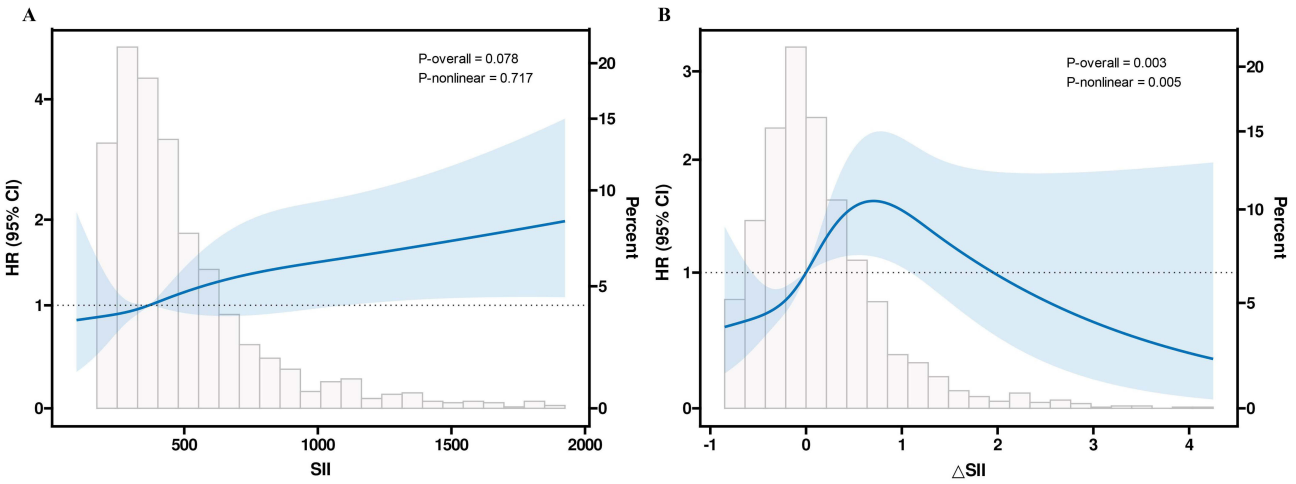

Figure 2 RCS analysis between SII /ΔSII and postoperative ACRN recurrence (HR, 95% *CI*). (**A**) SII and postoperative ACRN recurrence. (**B**) ΔSII and postoperative ACRN recurrence.

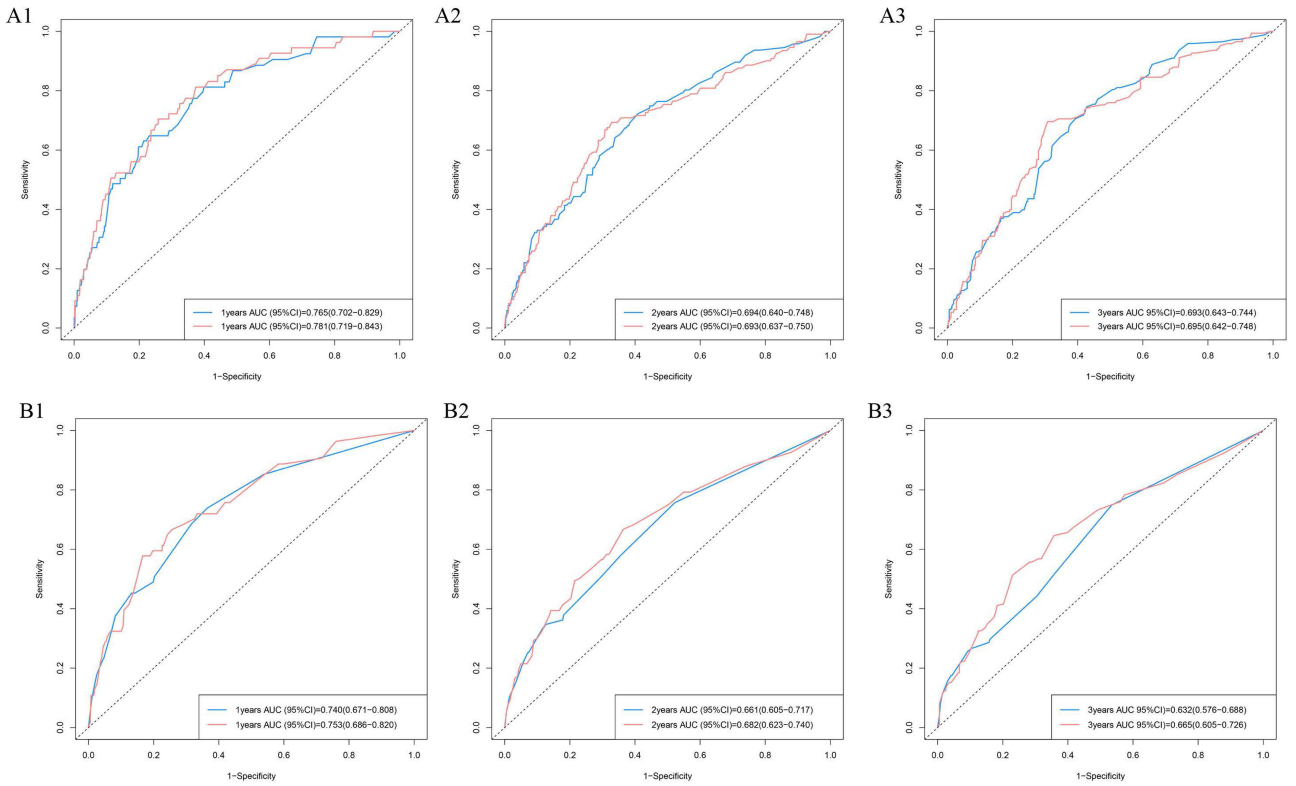

Figure 3 ROC curve of SII and its changes for ACRN recurrence after colorectal adenoma resection. (**A**) A1: ROC curve for 1-year recurrence. A2: ROC curve for 2-year recurrence. A3: ROC curve for 3-year recurrence.Blue line: ROC curve adjusted for confounding factors (adenoma number, adenoma size, and adenoma dysplasia grade); Red line: ROC curve incorporating both confounders and SII grouping. (**B**) B1: ROC curve for 1-year recurrence. B2: ROC curve for 2-year recurrence. B3: ROC curve for 3-year recurrence. Blue line: ROC curve adjusted for confounders (age, adenoma number, adenoma size, adenoma dysplasia grade, family history, and SII grouping); Red line: ROC curve incorporating both confounders and ΔSII grouping.

size, dysplasia grade), family history, and ΔSII grouping, the baseline model achieved AUC values of 0.740, 0.661, and 0.632 for 1, 2, and 3-year recurrence. And incorporation of ΔSII grouping further enhanced performance, with AUC values increasing to 0.753, 0.682, and 0.665, respectively (Figure 3B).

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Table 3 Subgroup Analysis of Association Between SII Levels and Changes and Postoperative ACRN Recurrence

	Q2		Q3		Q4		P for Interacion	ΔSII<-0.15		ΔSII>0.15		P for Interacion
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value		HR (95% CI)	*P* value	HR (95% CI)	*P* value	
Sex							0.755					0.137
Male	1.20 (0.68–2.13)	0.524	1.46 (0.83–2.58)	0.189	1.83 (1.05–3.21)	0.034		0.81 (0.46–1.45)	0.485	1.78 (1.08–2.95)	0.024	
Female	1.06 (0.45–2.49)	0.899	1.35 (0.61–2.98)	0.463	1.52 (0.69–3.33)	0.297		1.07 (0.47–2.40)	0.879	1.97 (0.91–4.28)	0.087	
Age							0.961					0.926
18-45	0.85 (0.20–3.60)	0.828	1.43 (0.39–5.18)	0.586	1.15 (0.27–4.85)	0.854		1.21 (0.19–7.80)	0.840	4.56 (0.90–23.03)	0.066	
45-60	1.18 (0.57–2.46)	0.653	1.36 (0.67–2.79)	0.398	1.61 (0.80–3.22)	0.181		0.99 (0.50–1.98)	0.983	1.40 (0.74–2.65)	0.307	
≥60	1.28 (0.62–2.62)	0.506	1.46 (0.72–2.97)	0.296	2.42 (1.22–4.78)	0.011		0.80 (0.40–1.61)	0.536	1.94 (1.05–3.57)	0.035	

Notes: SII grouping Analysis: Models were adjusted for age, adenoma number, adenoma size, adenoma dysplasia grade, and family history, with Q1 designated as the reference group. ΔSII Grouping Analysis: Models were adjusted for the above covariates plus baseline SII quartiles, using −0.15≤ ΔSII ≤0.15 as the reference group. Subgroup Methodology: Stratification variables (sex/age) were not included as additional adjustments in subgroup-specific models to avoid overadjustment.
Abbreviations: HR, hazard ratio; CI, confidence interval; Q2 group, 275.60≤ SII <368.07×10^9/L; Q3 group, 368.07≤ SII <513.62×10^9/L; Q4 group, SII ≥513.62×10^9/L.

Subgroup Analysis

Subgroup analyses stratified by age and sex consistently demonstrated elevated risks of ACRN recurrence in the ΔSII >0.15 and Q4 groups compared to their respective reference groups (−0.15 ≤ ΔSII ≤0.15 and Q1; all P<0.05). Among males, the ΔSII >0.15 group exhibited a 1.78-fold higher recurrence risk (95% *CI*, 1.08–2.95), while the Q4 group showed a 1.83-fold increase (95% *CI*, 1.05–3.21). In older adults (≥60 years), the ΔSII >0.15 group had a 1.94-fold elevated risk (95% *CI*, 1.05–3.57), and the Q4 group demonstrated a 2.42-fold higher risk compared to Q1 (95% *CI*, 1.22–4.78). In contrast, no significant associations were observed for ΔSII <0.15 or Q2-Q3 in females or younger adults (<60 years) (Table 3).

Sensitivity Analysis

In sensitivity analyses, excluding patients with ACRN recurrence within six months post-resection, both SII grouping and ΔSII grouping significant risk factors for ACRN recurrence in unadjusted and adjusted models (all P<0.05)(Table S4). These findings robustly confirm the strong association between SII change and postoperative ACRN recurrence risk.

Discussion

This study utilized repeated survey data from the same cohort at two time points to analyze the relationship between baseline SII levels, ΔSII during follow-up, and recurrent ACRN after adenoma resection. The results demonstrated that both high baseline SII levels and a significant increase in SII (ΔSII >0.15 group) were independent risk factors for ACRN recurrence after polypectomy.

Previous studies have established the prognostic value of SII in patients with CRC. Elevated preoperative SII levels are consistently associated with worse survival and increased recurrence risk after curative surgery. A study involving 181 patients undergoing radical CRC surgery found that the recurrence group had significantly higher SII levels than the non-recurrence group.[20] Furthermore, a prospective cohort study reported that every 100-unit increase in SII elevated postoperative tumor recurrence risk by 24.4%, and an SII ≥513.53×10^9/L was associated with poorer overall survival.[21] The underlying mechanisms may involve the systemic inflammatory state reflected by elevated SII, which promotes tumorigenesis through the activation of NF-κB and STAT3 signaling pathways.[22] Additionally, platelet components in SII may facilitate residual adenoma cell proliferation and angiogenesis through release of pro-angiogenic factors such as TGF-β and VEGF.[23,24]

However, evidence regarding the role of SII specifically in the recurrence risk of colorectal adenoma is limited. A critical knowledge gap exists in understanding whether SII can predict the recurrence of adenomas after resection. Recent research has begun to address the association between SII and adenoma risk. A 2025 cross-sectional study involving over 3000 individuals identified a significant, non-linear (inverted U-shaped) relationship between SII and the prevalence of colorectal adenomas, highlighting the potential relevance of SII in the early stages of colorectal carcinogenesis.[25] Another diagnostic study from 2023 found that SII levels were significantly higher in patients with

early-stage CRC compared to those with adenomatous polyps,[26] further supporting the role of SII in marking disease progression along the adenoma-carcinoma sequence. Evidence linking both baseline SII and its change to ACRN recurrence after resection is limited, highlighting a critical gap in knowledge.

This study investigated the relationship between ΔSII and ACRN recurrence by categorizing the ΔSII, which demonstrated greater sensitivity to subtle fluctuations in patients with low baseline SII compared to absolute SII increments. After adjusting for potential confounders, the association between the ΔSII >0.15 group and ACRN recurrence post-polypectomy remained statistically significant (P <0.05). When both SII grouping and ΔSII grouping were incorporated into the model, both retained significance as independent predictors, reflecting dual mechanistic insights: First, SII serves as a critical biomarker for assessing ACRN progression, with elevated levels correlating with increased recurrence risk; second, longitudinal SII variations may more sensitively mirror dynamic shifts in the inflammatory and immune landscape, thereby acting as an early warning signal. This finding is strongly supported by emerging longitudinal evidence in colorectal cancer. A longitudinal study of 817 CRC patients with serial measurements demonstrated that the pathological evolution of SII over time served as a valuable prognostic indicator, independent of single-timepoint values.[27] Our results are consistent with this principle and extend its relevance to the precancerous stage. Similarly, Zhou et al identified postoperative SII trajectories as pivotal prognostic indicators in colorectal cancer patients,[28] further validating the clinical relevance of monitoring inflammatory dynamics in predicting tumor outcomes

This study identified age, baseline adenoma size, baseline dysplasia grade, SII grouping, and ΔSII grouping as independent risk factors for ACRN recurrence after colorectal adenoma resection through multivariate Cox proportional hazards regression analysis, not only validating established predictors from prior research but also highlighting the potential role of dynamic systemic inflammatory changes in adenoma recurrence. The associations between traditional pathological indicators (age, adenoma size ≥10 mm, and high-grade dysplasia) and ACRN recurrence have been widely confirmed,[29,30] with current guidelines designating adenomas >10mm as high-risk lesions,[31,32] supported by a long-term follow-up study showing a 2.6-fold increased recurrence risk for adenomas ≥10 mm compared to smaller ones,[33] while high-grade dysplasia was recognized as an independent predictor of postoperative ACRN and CRC,[34] aligning with our findings that emphasize the importance of baseline lesion characteristics in risk stratification. Furthermore, the predictive value of SII grouping reinforces the critical role of inflammatory microenvironments in colorectal tumorigenesis. Innovatively introducing SII change rate as a dynamic biomarker, this study revealed its significant association with ACRN recurrence risk (P <0.05), suggesting that persistent postoperative inflammatory escalation may accelerate residual adenoma progression through mechanisms such as epithelial-mesenchymal transition or immunosuppression,[35] a finding consistent with the "inflammation-carcinogenesis cycle" hypothesis in tumor microenvironments.[11]

SII has the potential to serve as a convenient blood biomarker for risk stratification management following colorectal adenoma resection. To facilitate the clinical translation of our findings, we propose a testable hypothesis: periodic monitoring of SII dynamics could enable early warning of adenoma recurrence. Future research should focus on establishing standardized "alert thresholds" for ΔSII through multi-center prospective studies using time-dependent ROC analysis, validating these thresholds in sufficiently large cohorts (typically involving thousands of participants), and exploring the most feasible clinical integration pathway—utilizing ΔSII to optimize colonoscopy surveillance intervals. Ultimately, decision-curve analysis should be employed to evaluate the incremental clinical benefit and cost-effectiveness of this biomarker-stratified strategy compared to the current fixed-interval surveillance paradigm.

Limitations

This study has several limitations: First, numerous laboratory parameters were analyzed, and hematological indicators—particularly SII components—may fluctuate due to temporal variations, medication use, and lifestyle factors; second, the single-center recruitment design may limit generalizability across diverse populations,regional and ethnic variations); third, SII change rates were calculated from only two measurements (preoperative and postoperative), which may not capture granular longitudinal dynamics, future investigations should incorporate serial measurements at multiple time-points to refine trajectory analyses.

Conclusion

This study confirms that the SII and its dynamic increase during follow-up are associated with an independently increased risk of ACRN after adenoma resection. This finding underscores the potential role of systemic inflammation, as reflected by SII, in the context of precancerous lesion progression, and suggests that monitoring SII dynamics may offer higher prognostic value than a single measurement. The developed nomogram serves as a preliminary visual tool for risk communication. The more profound significance of this study provides a pathway for translating SII, an easily accessible composite inflammatory marker, into a routine clinical monitoring tool. This requires validation through large-scale prospective cohort studies to establish standardized early-warning thresholds for its longitudinal changes. In the future, this tool could help identify patients at high risk of recurrence after polypectomy, thereby providing a basis for more personalized and efficient colonoscopy surveillance strategies and ultimately contributing to the early prevention of colorectal cancer.

Data Sharing Statement

The datasets analysed during the current study are included in this published article. No additional data will be shared.

Ethics Approval and Consent to Participate

This study was reviewed and approved by Institutional Review Board of the First Affiliated Hospital of Zhengzhou University (ethical review number: 2022-KY-0018-002) and all the participants signed the informed consent requirement. This study complied with the Declaration of Helsinki.

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Author Contributions

Yujie Sun: Conceptualization (lead); Data curation (lead); Formal analysis (lead); Methodology (lead); Writing - original draft (lead). Jingfeng Chen: Conceptualization (equal); Data curation (equal); Funding acquisition (equal); Methodology (equal); Supervision (equal); Writing - review & editing (equal). Jiaoyan Li: Data curation (lead); Writing - review & editing (supporting); Supervision (supporting); Methodology (supporting). Jianan Shao: Data curation (lead); Writing - review & editing (supporting). Weikang Li: Data curation (lead); Writing - review & editing (supporting). Suying Ding: Conceptualization (lead); Funding acquisition (lead); Supervision (lead); Writing - review & editing (lead). All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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